Remarks

Claims 1-26 were pending in the subject application. By this Amendment, the applicants have amended claims 18, 20- 22, and 24-26 and have canceled claim 19. In addition, claims 1-17 have been canceled as being directed to non-elected subject matter. No new matter has been added by these amendments. Support for the amendments can be found throughout the subject specification including, for example, at page 8, lines 29-33, page 12, lines 4-11, page 17, lines 19-29, and Example 1, Table 2. Accordingly, claims 18 and 20-26 are currently before the Examiner for consideration. Favorable consideration is respectfully requested.

The amendments presented herein have been made to lend greater clarity to the claimed subject matter and to expedite prosecution of the subject application to completion. These amendments should not be construed as an indication of the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claims 18-19 and 22-25 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. As an initial matter, claim 19 has been canceled, thus rendering moot the rejection of this claim. The applicants respectfully traverse this ground for rejection to the extent that it might be applied to the claims now presented for examination.

The claims have been amended herein to more clearly focus on the use of certain specific compounds. Specifically, the claims now recite that the method comprises the administration of cysteamine, or a salt thereof. The use of these compounds is explicitly set forth in the specification as filed thereby providing ample evidence of the inventors' possession of the claimed invention at the time of filing. Accordingly, the applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §112, first paragraph.

Claims 18-22 and 24-26 have been rejected under 35 U.S.C. §102(b) as being anticipated by Benton *et al.* (U.S. Patent No. 5,605,885). The applicants respectfully traverse this rejection to the extent that it might be applied to the claims now presented for examination.

As noted above, the claims have been amended herein in order to lend greater clarity to the claimed subject matter. In this context, the claims now specifically recite the use of cysteamine

and/or salts thereof ***in maintaining or lowering cortisol levels*** in a patient following a stressful event. The Benton *et al.* reference does not teach or suggest using cysteamine in maintaining or lowering cortisol levels in a patient.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra; Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

Benton *et al.* fail to teach administering cysteamine, or a salt thereof, to a patient ***prior to a stressful event*** in order to maintain or reduce cortisol in the patient following the stressful event. Rather, Benton *et al.* teach methods for treating *immunosuppressed patients* by administering prolactin or compounds that have prolactin-like activity (such as cysteamine) to:

> 1) up-regulate expression of prolactin receptors when administered to the whole animal, or 2) to stimulate growth of the NB-2 rat lymphoma cell line, a standard bioassay for prolactin activity, or 3) to substitute for prolactin to support mammalian lactation, and either a) stimulate the proliferative responses of spleen or peripheral blood lymphocytes co-cultured with mitogens following 72 hours of continual hormone or drug administration (i.e. in laboratory mice); or b) reverse the suppression of lymphocyte proliferative responses to mitogens in spleen lymphocytes of mice treated simultaneously with 125 μg/day of corticosterone and a reasonable dose (5 to 200 μg/day) of the prolactin-like protein or the prolactin agonist drug. (Col. 7, lines 56-67)

See also claims 1-20; col. 4, lines 7-22; and col. 8, line 57 through col. 9, line 2. The Benton *et al.* reference has no teaching or suggestion regarding the ability of cysteamine, when administered to a patient prior to a stressful event, to maintain or lower cortisol levels following the stressful event. The authors describe the use of prolactin to increase prolactin receptors and stimulate lymphocyte

proliferation (see, for example, col. 10 line 45 through col. 11, line 17 and Examples 1-13) in *immunosuppressed patients*. The authors also describe administering prolactin to immunosuppressed patients following exogenous adrenal corticosteroid treatment, wherein such treatment impairs the patient's ability to secrete endogenous steroid hormones, such as cortisol (see, col. 3, lines 53-56). The authors teach that by administering prolactin (or cysteamine) to patients chronically treated with exogenous glucocorticosteroids, adrenal cortical secretory functions can be restored, thus enabling the patient to ***increase*** cortisol levels (see, col. 3, lines 53-62, col. 5, lines 40-44; col. 8, lines 29-32; col. 10, lines 10-24; and Example 2). Therefore, it is very difficult to draw conclusions from the Benton *et al.* article about the ability of cysteamine (or a salt thereof), when preemptively administered to a patient prior to a stressful event, to reduce or maintain cortisol levels in the patient following a stressful event. In fact, the findings of Benton *et al.* essentially teach away from the methods of the claimed invention.

The applicants further respectfully point out that for a claim to be anticipated under the principles of inherency, the subject of a single prior art reference must necessarily function in accordance with the limitations of the process or method claimed. *In re King*, 801 F2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). Further,

> the doctrine of inherency is available only when the prior inherent event can be established as a certainty. That an event may result from a given set of circumstances is not sufficient to establish anticipation. . . . A prior inherent event cannot be established based on speculation, or where a doubt exists (emphasis added). *Ethyl Molded Product Co. v. Betts Package Inc.*, 9 USPQ 2d 1001, 1032-33 (E.D. KY 1988).

Since Benton *et al.* essentially teach administering cysteamine to ***ensure*** adrenal sufficiency, including the ability to increase cortisol levels in the immunosuppressed patient, it cannot be said that the Benton *et al.* reference inherently teaches methods for ***maintaining or reducing cortisol levels*** in a patient following a stressful event. Therefore, Benton *et al.* does not disclose or suggest the applicants' method, as currently claimed. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the Benton *et al.* reference.

Claim 23 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Benton *et al.* in view of McCleary (U.S. Patent No. 6,964,969). The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not disclose or suggest the claimed subject matter.

The subject invention is directed to methods for maintaining or lowering cortisol in a patient following a stressful event. The Office Action asserts that Benton *et al.* discloses the methods of the subject invention except for the stress reducing therapies taught by McCleary. The applicants respectfully disagree. The arguments presented above that Benton *et al.* do not teach the claimed invention are reasserted herein.

To summarize, the current invention is in contrast to the teachings of Benton *et al.*, which require administering cysteamine to an ***immunosuppressed patient*** to stimulate increased prolactin levels in the patient, thus stimulating the immune system. The basis for the Benton *et al.* treatment is attributed to "increases in prolactin receptors...[that are] found to correlate directly with the change in immune responsiveness...."col. 10, lines 53-57 and to making "the lymphocyte better able to proliferate in response to immune stimuli." Col. 11, lines 5-6.

There is no description or teaching whatsoever by Benton *et al.* regarding the ability of cysteamine to lower cortisol levels, let alone a method for maintaining or lowering cortisol levels in a patient following a stressful event. McCleary does not cure or even address the deficiencies identified in the Benton *et al.* reference. Specifically, McCleary fails to teach or suggest administering cysteamine, or a salt thereof, to a patient to maintain or lower cortisol levels should the patient encounter a stressful event.

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.*

Morever, as expressed by the CAFC, to support a §103 rejection, "[b]oth the suggestion and the expectation of success must be founded in the prior art ..." *In re Dow Chemical Co.* 5 USPQ 2d 1529, 1531 (Fed. Cir. 1988). One finds neither the suggestion nor the expectation of success in the cited references, either separately or combined.

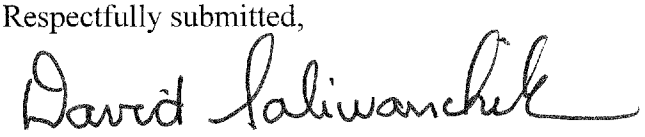
Because Benton *et al.* and McCleary fail to teach or suggest combining cysteamine with another therapy for stress, or that this combination would produce an excellent therapeutic effect (that being maintaining or lowering cortisol levels in the patient following a stressful event), the subject invention cannot be said to be obvious. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a)

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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